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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/607,358	06/26/2003	Eduardo M. Lasalvia-Prisco	1.241.03	6124

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MALLOY & MALLOY, P.A.
Historic Coral Way
2800 S.W. Third Avenue
Miami, FL 33129

EXAMINER	
SANG, HONG	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/607,358	LASALVIA-PRISCO, EDUARDO M.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *1-59 and 66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/10/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

RE: Lasalvia-Prisco

1. Applicant's election without traverse of Group III (claims 60-65) in the reply filed on 2/22/06 is acknowledged.

2. The information disclosure statement (IDS) filed on 6/10/2004 has been considered. A signed copy is attached hereto.

3. Claims 1-66 are currently pending. Claims 1-59 and 66 are withdrawn from further consideration as being drawn to non-elected inventions.

4. Claims 60-65 are under examination.

Claim Rejections - 35 USC § 112, 2nd paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 60-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The recitation of "a supernatant plasma-cell layer", "plasma-cell solution" and "plasma-cell fraction" in claims 60 and 62–65 is indefinite because the meaning of "a supernatant plasma-cell layer", "plasma-cell solution" and "plasma-cell fraction" is unclear. Does the "plasma-cell" mean the supernatant (plasma layer) and the interface cell layer (buffy coat) of the blood? Or it means the supernatant (plasma), interface cell layer and red blood cells (bottom layer).

B. The recitation of "fractioning" in claims 60 and 65 is indefinite. The "fractioning" usually means separating a mixture on the basis of some property or properties of its components, for example, by molecular weight, or charge state, etc. It is unclear how to fractioning a sample just by heating, which does not involve a separation step.

C. The recitation of "a blood specimen solution" in claim 60 is indefinite because it is unclear how to form a blood specimen solution. The claim only recites the step "extracting a blood specimen from the patient" (see line 5 of claim 60). What is a blood specimen solution? How to make the blood specimen solution? Is it a blood sample?

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 60-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lasalvia et al. (31st annual meeting of the ASCO, May, 1995, A730) in view of Moingeon et al. (Vaccine 2001 (Jan), 19: 1305-1326), Ryan (US Patent No. 4,436,821, 5/13/1984), Freshney (Freshney, Culture of Animal Cells, A Manual of Basic Technique, 4th Edition, 2000, pages 423-424), Somani (US Patent No. 3,906,107, 9/16/1975), Colaco (US 2005/0175635 A1, effective filing date at least 2/22/2001), Moore (US Patent No. 5,328,844, 7/12/1994), Mejza (US Patent No. 6,416,992 B1, effective filing date at least 10/13/1999), Heldebrant (US Patent No. 4,490,361, 12/25/1984).

Due to the indefinite nature of claims 60-65 (see paragraph 6 above), the "plasma-cell layer" and "plasma-cell solution" are interpreted as plasma and interface cells layer (buffy coat), and the "blood specimen solution" is interpreted as blood sample.

Claims 60-65 are drawn to a method of preparation of an autologous hemoderivative composition for use eliciting an effective antitumoral immune response in a patient comprising: extracting a blood specimen from the patient and forming a blood specimen solution, collecting the plasma and interface cells from the blood specimen solution after settling, diluting the plasma and interface cells in a dilutant forming a plasma and interface cells solution and thereby inducing a hypotonic shock, cooling and heating the plasma and interface cells solution and thereby inducing a hypothermic shock, heating the plasma and interface cells solution to a predetermined temperature for a predetermined period of time, and filtering the plasma and interface cells prior to administrating to the patient.

Claims are further limited wherein the method further comprises extracting approximately 20 milliliters of the blood specimen from the femoral artery of the patient into a heparin solution thereby forming the blood specimen solution, settling the blood specimen solution for approximately one hour and separating the plasma and interface cells layer, diluting plasma and interface cells in distilled water at a ratio in an range of approximately 3-4 parts distilled water per I part plasma and interface cells, cooling the plasma and interface cells solution to approximately minus twenty degrees centigrade for approximately 24 hours, heating plasma and interface cells solution to

approximately one hundred degrees centigrade for between approximately 8 to 10 minutes.

Claims are interpreted to be a method for preparing a mixture of blood plasma and interface cell lysate. However, the preparation of blood plasma and interface cell lysate is well known in the art as shown by the following references.

Lasalvia teaches a method of treating metastatic cancer using autologous blood fraction from cancer patients (see the abstract).

Lasalvia does not teach how to make the autologous blood fraction from cancer patients. However, these deficiencies are made up for in the teachings of Moingeon, Ryan, Freshney, Somani, Colaco, Moore, Mejza, and Heldebrant.

Moingeon teaches various kinds of cancer vaccine including whole cell preparations, for example, tumor cells, cytotoxic immune cells, antigen presenting cells, as well as tumor lysates derived from autologous or allogenic tumor cell lysates (see abstract, page1306, left column, page 1307, right column, last paragraph, and page 1317, Table 4). Moingeon teaches cell extracts or semi-purified proteins-based cancer vaccines for example secreted proteins or membrane fragments (large multivalent imunogens) (see page 1309, left column). Moingeon teaches the tumor associated antigen-based vaccines (see page 1306, right column, last paragraph, and page 1309, right column). Moingeon teaches that human tumor antigens are present in the serum (see page 1311, left column). Moingeon teaches vaccines targeting multiple tumor associated antigens, and/or in association with adjuvant or immunositmulatory cytokines (see abstract, and page 1313, 3rd paragraph).

Ryan teaches that blood plasma and interface cells can be prepared from a blood sample by mixing the blood with an anticoagulant and separating from red blood cells using any of the conventional methods such as centrifugation or settling (see US Patent NO. 4,436,821, column 3, lines 40-45).

Freshney teaches isolation of the plasma and interface cells of the blood using heparin and centrifugation (see page 423).

Somani teaches collecting blood samples for plasma electrolytes and inulin measurements from the femoral artery of a dog (see column 2, example 1).

Colaco teaches a method of preparing cell lysate comprising: resuspend cells in a hypotonic buffer, disrupt cells using a homogenizer or by repeated freeze-thaw cycles, and remove the nuclear and cell debris by a high speed centrifugation (see column 4, paragraph [0039]).

Moore teaches lysing cells with equal volume of distilled water (see column 27, lines 17-20).

Mejza teaches lysing cells by three successive rounds of freezing and thawing, wherein freeze/thaw lysate is prepared by freezing and thawing the cell suspension 3 times by alternating between a dry ice/ethanol bath (until the cells are completely frozen) and a 37°C water bath (until completely thawed). Mejza teaches that the adenovirus presented in the cells can be heat inactivated by incubating the freeze/thaw lysate at 56°C for 1hr and any precipitate that forms during the heat inactivation is removed by centrifuging the sample (see column 1, lines 14-28). Mejza teaches that the lysate can be stored at –70°C.

Heldebrant teaches heat inactivation of infectious agents contained in plasma and in protein fractions separated from such plasma at 60-100°C, for 5-30 min for example (see column 1, lines 41-49, and claim 3). Heldebrant teaches filtering protein solution through a sterilized bacteria-retention membrane or cartridge filter to form a sterile bulk solution (see the bridging paragraph of columns 3 and 4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make an autologous hemoderivative composition comprising plasma and interface cell lysate in view of the teachings of Lasalvia and Moingeon. One would have been motivated to make an autologous hemoderivative composition comprising plasma and interface cell lysate because Lasalvia teaches an autologous blood fraction is effective in treating metastatic cancer, it is well know in the art that plasma contains various cytokines and growth factors, and Moingeon teaches that serum of the cancer patient also contains tumor associated antigen and the cancer vaccines comprising cell lysates, multiple tumor associated antigens, or tumor antigens in combination with cytokines are known in the art. One of ordinary skill in the art would have a reasonable expectation of success to make an autologous hemoderivative composition because the method of isolation of plasma and cell lysate from the interface cells are well known in the art as shown by the teachings of Ryan, Freshney, Somani, Colaco, Moore, Mejza, and Heldebrant.

While the above references do not specifically teach extracting 20 ml of the blood from a patient (see claim 61), settling the blood specimen for 1 hour (see claim 62), diluting the plasma and interface cell layer in distilled water at approximately ratio of 1:3

to 1:4 (see claim 63, Moore teaches 1:1), cooling the plasma and interface cells solution to –20°C for approximately 24 hours (see claim 64, Mejza teaches till completely frozen or store at –70°C), claims 61-65 are considered an obvious variation of the reference teaching absent a showing of unobvious property. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

Conclusion

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hong Sang
Art Unit 1643
Apr. 10, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER